

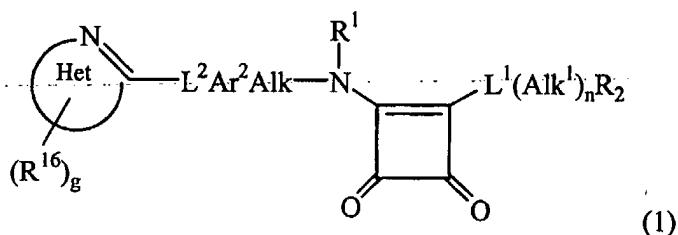
DOCKET NO.: CELL-0113
Application No.: 09/899,488
Office Action Dated: August 7, 2003

PATENT
REPLY FILED UNDER EXPEDITED
PROCEDURE PURSUANT TO
37 CFR § 1.116

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims:

1. (currently amended) A compound of formula (1):



wherein

Het is a bicyclic fused ring heteroaromatic group;

g is zero or the integer 1, 2, 3 or 4;

Each R¹⁶, which may be the same or different, is an atom or group -L³(Alk²), L⁴(R⁴)_u,

L³ and L⁴, which may be the same or different, are each a covalent bond or a linker atom or group -O-, -S-, -C(O)-, -C(O)O-, -OC(O)-, -C(S)-, -S(O)-, -S(O)₂-, -N(R⁸)-, -N(R⁸)O-, -N(R⁸)N-, -CON(R⁸)-, -OC(O)N(R⁸)-, -CSN(R⁸)-, -N(R⁸)CO-, -N(R⁸)C(O)O-, -N(R⁸)CS-, -S(O)₂N(R⁸)-, -N(R⁸)S(O)₂-, -N(R⁸)CON(R⁸)-, -N(R⁸)CSN(R⁸)-, or -N(R⁸)SO₂N(R⁸)-,

R⁸ is a hydrogen atom or an optionally substituted C₁₋₆alkyl group,

t is zero or the integer 1,

u is an integer 1, 2 or 3,

Alk² is an aliphatic or heteroaliphatic chain, and

R⁴ is a hydrogen or halogen atom or a group selected from an optionally substituted C₁₋₆alkyl or C₃₋₈ cycloalkyl group, -OR⁵ (where R⁵ is a hydrogen atom, an optionally

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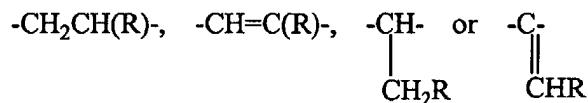
substituted C₁₋₆alkyl or C₃₋₈ cycloalkyl group), -SR⁵, -NR⁵R⁶ (where R⁶ is as just defined for R⁵ and may be the same or different), -NO₂, -CN, -CO₂R⁵, -SO₃H, -SOR⁵, SO₂R⁵, -SO₃R⁵, -OCO₂R⁵, -CONR⁵R⁶, -OCONR⁵R⁶, -CSNR⁵R⁶, -COR⁵, -OCOR⁵, -N(R⁵)COR⁶, -N(R⁵)CSR⁶, -SO₂N(R⁵)(R⁶), -N(R⁵)SO₂R⁶, N(R⁵)CON(R⁶)(R⁷) (where R⁷ is a hydrogen atom, an optionally substituted C₁₋₆alkyl or C₃₋₈cycloalkyl group), -N(R⁵)CSN(R⁶)(R⁷) or -N(R⁵)SO₂N(R⁶)(R⁷),

provided that when t is zero and each of L³ and L⁴ is a covalent bond then u is the integer 1 and R⁴ is other than a hydrogen atom;

L² is a covalent bond or an atom or group -O-, -S-, -C(O)-, -C(S)-, -S(O)-, -S(O)₂, -N(R⁸)- or -C(R⁸)(R^{8a})- (where R^{8a} is an atom or group as defined for R⁸ and may be the same or different);

Ar² is an optionally substituted aromatic or heteroaromatic group;

Alk is a chain



in which R is a carboxylic acid (-CO₂H), a carboxylic acid ester, a carboxylic acid amide, or a carboxylic acid biostere;

R¹ is a hydrogen atom or a C₁₋₆alkyl group;

L¹ is a covalent bond or a linker atom or group -O-, -S-, -C(O)-, -C(O)O-, -OC(O)-, -C(S)-, -S(O)-, -S(O)₂-, -N(R⁸)-, -N(R⁸)O-, -N(R⁸)N-, -CON(R⁸)-, -OC(O)N(R⁸)-, -CSN(R⁸)-, -N(R⁸)CO-, -N(R⁸)C(O)O-, -N(R⁸)CS-, -S(O)₂N(R⁸)-, -N(R⁸)S(O)₂-, -N(R⁸)CON(R⁸)-, -N(R⁸)CSN(R⁸)-, or -N(R⁸)SO₂N(R⁸)-;

Alk¹ is an optionally substituted aliphatic chain;

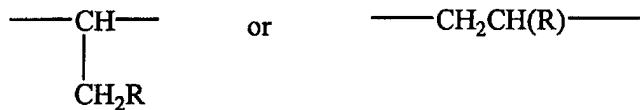
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n is zero or the integer 1;

R^2 is a hydrogen atom or an optionally substituted heteroaliphatic, C_{3-10} cycloalkyl, C_{3-10} cycloalkenyl, C_{3-10} heterocycloalkyl, C_{3-10} heterocycloalkenyl, C_{7-10} bicycloalkyl, C_{7-10} tricycloalkyl, C_{7-10} bicycloalkenyl, C_{7-10} tricycloalkenyl, C_{7-10} bicycloheteroalkyl, C_{7-10} tricycloheteroalkyl, C_{7-10} bicycloheteroalkenyl, C_{7-10} tricycloheteroalkenyl, C_{3-10} cycloaliphatic, C_{3-10} heterocycloaliphatic, C_{7-10} polycycloaliphatic, C_{7-10} heteropolycycloaliphatic, aromatic or heteroaromatic group, wherein said heteroaliphatic, heterocycloalkyl, heterocycloalkenyl, bicycloheteroalkyl, tricycloheteroalkyl, bicycloheteroalkenyl and tricycloheteroalkenyl C_{3-10} heterocycloaliphatic, and C_{7-10} heteropolycycloaliphatic groups contain one, two, three, or four heteroatoms or heteroatom-containing groups as defined for L^3 and L^4 , which may be the same or different; provided that Het is not a 2,6-naphthyridin-1-yl, isoquinolin-1-yl, 2,7-naphthyridin-1-yl or quinazolin-4-yl group; and the salts and N-oxides thereof.

2. (original) A compound according to Claim 1 in which Alk is a chain



3. (original) A compound according to Claim 1 in which R is a carboxylic acid ($-\text{CO}_2\text{H}$) group.

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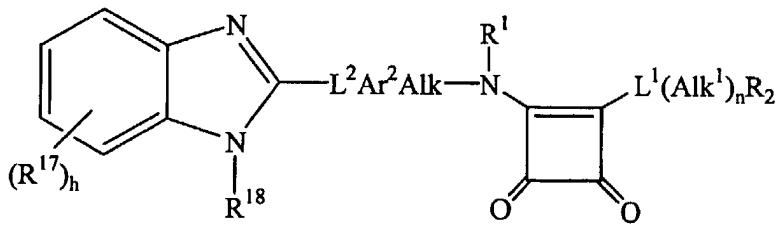
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4. (original) A compound according to Claim 1 in which R is an esterified carboxyl group of formula -CO₂Alk⁷.
5. (original) A compound according to Claim 1 in which R¹ is a hydrogen atom.
6. (original) A compound according to Claim 1 in which Ar² is an optionally substituted phenylene group.
7. (original) A compound according to Claim 1 in which L¹ is a -N(R⁸)- group where R⁸ is a hydrogen atom or an optionally substituted C₁₋₆alkyl group.
8. (original) A compound according to Claim 7 in which R⁸ is a methyl, ethyl, or n-propyl group.
9. (original) A compound according to Claim 1 in which L¹ is a covalent bond.
10. (original) A compound according to Claim 1 in which n is the integer 1, Alk¹ is an optionally substituted straight or branched C₁₋₆alkylene chain and R² is a hydrogen atom.
11. (original) A compound according to Claim 10 in which Alk¹ is a -CH₂-, -CH₂CH₂-, -CH₂CH₂CH₂-, -CH(CH₃)CH₂- or -C(CH₃)₂CH₂- chain.

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12. (currently amended) A compound according to Claim 1 in which L¹ is a covalent bond, n is zero and R² is an optionally substituted C₅₋₇heterocycloalkyl or C₅₋₇heterocycloalkenyl C₅₋₇heterocycloaliphatic group.
13. (original) A compound according to Claim 12 in which R² is an optionally substituted piperidinyl, homopiperidinyl, heptamethyleneiminy, pyrrolidinyl, piperazinyl, homopiperazinyl, morpholinyl or thiomorpholinyl group.
14. (original) A compound according to Claim 1 in which L² is an -O- atom or -N(R⁸)- group in which R⁸ is a hydrogen atom or an optionally substituted C₁₋₆alkyl group.
15. (previously presented) A compound according to Claim 1 of formula (2a):



wherein:

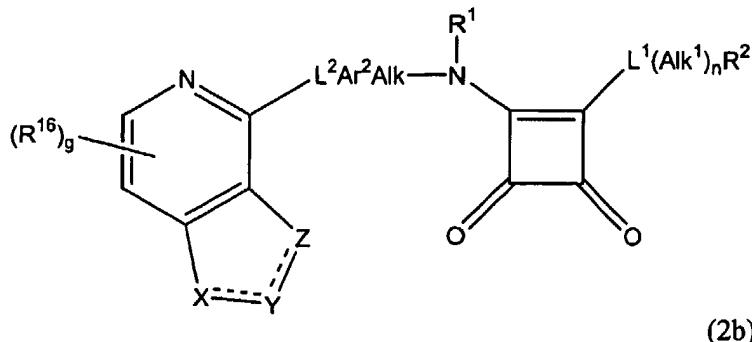
R¹⁷ is an atom or group R¹⁶ as previously defined;

h is zero or the integer 1, 2 or 3;

R¹⁸ is a hydrogen atom or an atom or group R¹⁶ as previously defined;
and the salts and N-oxides thereof.

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16. (previously presented) A compound according to Claim 1 of formula (2b):



wherein:

X, Y and Z are each independently selected from a nitrogen, oxygen or sulphur atom or CH group;

the broken line (---) represents saturation or unsaturation;

and the salts and N-oxides thereof.

17. (original) A compound according to Claim 16 in which X is an O or S atom, Y and Z are each a group CH, a single bond joins X and Y and a double bond joins Y and Z.

18. (currently amended) A compound according to Claim 16 in which Z is an O or S atom, X and Y is are each a CH group, a single bond joins Y and Z and a double bond joins X and Y.

19. (previously presented) A compound which is:

S-2-{[2-Dipropylamino)-3,4-dioxo-1-cyclobutenyl]amino}-3-{4-[(1-methylbenzimidazol-2-yl)amino]phenyl}propanoic acid;

S-2-{[2-Dipropylamino)-3,4-dioxo-1-cyclobutenyl]amino}-3-{4-[(1-methylbenzimidazol-2-yl)amino]phenyl}propanoic acid;

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S-2-{{2-(2-Methylpiperidin-1-yl)-3,4-dioxo-1-cyclobut enyl]amino}-3-{4-[(1-methylbenzimidazol-2-yl)amino]phenyl}propanoic acid;

(S)-3-[4-(Thiophen[2,3-d]pyrimidin-4-ylamino)phenyl]2-(2-(diethylamino-3,4-dioxocyclobut-1-enylamino)propanoic acid;

and the salts, N-oxides and carboxylic acid esters thereof.

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20. (original) A pharmaceutical composition comprising a compound according to Claim 1 together with one or more pharmaceutically acceptable carriers, excipients or diluents.

21. (previously presented) A method for the treatment of inflammatory arthritis, allograft rejection, diabetes, inflammatory dermatoses, asthma or inflammatory bowel disease comprising administering to a mammal suffering from such a disease or disorder a therapeutically effective amount of a compound according to Claim 1.

22. (canceled)

23. (previously presented) A method according to Claim 21 wherein said inflammatory arthritis is selected from the group consisting of rheumatoid arthritis, vasculitis and polydermatomyositis.

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24. (previously presented) A method according to Claim 21 wherein said inflammatory dermatoses are selected from the group consisting of psoriasis and dermatitis.

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25. (canceled)

26. (canceled)

27. (previously presented) A compound according to claim 19 wherein the carboxylic acid esters are selected from the group consisting of methyl, ethyl, propyl, and i-propyl.

Filing Date

7/5/02

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10/ R99,462

Paper

3 S ~~1/6/03~~
11 - 6/4/03

Title ✓

Abstract ✓

Oath ✓

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Application

0016775
0024364,8

filed 7/2/00
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IDS

3 ≠ #7

Drawings

None

Number of claims

Claim 25, 26 twenty-five four

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